

## CLAIMS

### What is claimed is:

1. A method of imaging *in vivo* expression of a gene in a brain cell of a vertebrate, said method comprising:

5 i) administering to said vertebrate an imaging reagent comprising a detectable label attached to a first nucleic acid that specifically hybridizes to a second nucleic acid transcribed from said gene, where said first nucleic acid is linked to a targeting ligand that binds a receptor on a cell comprising the blood brain barrier of said vertebrate and crosses said blood brain barrier; and

10 ii) detecting the presence or quantity of a signal produced by said detectable label in said brain cell where the presence or quantity of said label indicates the presence or quantity of a nucleic acid transcribed from said gene or cDNA.

2. The method of claim 1, wherein said nucleic acid is a peptide nucleic acid (PNA).

15 3. The method of claim 1, wherein said targeting ligand is selected from the group consisting of an antibody that specifically binds to a receptor on a cell comprising the blood brain barrier, and a substrate specifically bound by a receptor on a cell comprising the blood brain barrier.

20 4. The method of claim 3, wherein said targeting ligand is selected from the group consisting of insulin, transferrin, insulin-like growth factor I (IGF-I), insulin-like growth factor II (IGF-II), basic albumin, leptin, and prolactin.

25 5. The method of claim 3, wherein said targeting ligand is an antibody that specifically binds to a receptor selected from the group consisting of an insulin receptor, a transferrin receptor, an insulin-like growth factor I (IGF-IR) receptor, and insulin-like growth factor II receptor (IGF-IIR), and a leptin receptor.

6. The method of claim 1, wherein said first nucleic acid is linked to said targeting ligand by a linker or by an affinity tag.

7. The method of claim 1, wherein said first nucleic acid is linked to said targeting ligand by an affinity tag comprising a biotin and a molecule that binds to biotin.

5 8. The method of claim 7, wherein said molecule that binds to biotin is selected from the group consisting of an avidin, a streptavidin, and an anti-biotin antibody.

9. The method of claim 7, wherein said first nucleic acid is a peptide nucleic acid.

10. The method of claim 9, wherein the carboxyl terminal of said first nucleic acid is amidated.

10 11. The method of claim 7, wherein said first nucleic acid is an antisense peptide nucleic acid.

12. The method of claim 7, wherein said first nucleic acid bears a protecting group.

15 13. The method of claim 7, wherein said first nucleic acid is a peptide nucleic acid having an amidated carboxyl terminal.

14. The method of claim 1, wherein said detectable label is selected from the group consisting of an radioactive label, a magnetic label, a spin label, an enzymatic label, a colorimetric label, and a fluorescent label.

20 15. The method of claim 1, wherein said nucleic acid is labeled with a radiolabeled amino acid.

16. The method of claim 15, wherein said radiolabeled amino acid is a tyrosine labeled with  $^{125}\text{I}$ .

17. The method of claim 15, wherein said radiolabeled amino acid is a lysine labeled with  $^{111}\text{indium}$ .

18. The method of claim 1, wherein said gene is a gene that encodes a molecule selected from the group consisting of a receptor, and enzyme, a structural protein, and a transcription factor.

5 19. The method of claim 1, wherein:  
said first nucleic acid is a peptide nucleic acid;  
said targeting ligand is an antibody that specifically binds to a receptor on a cell comprising the blood-brain barrier; and  
said first nucleic acid is attached to said targeting ligand through an affinity tag.

10 20. The method of claim 19, wherein said antibody is a monoclonal antibody.

21. The method of claim 20, wherein said imaging reagent comprises a radioactive label or a magnetic label.

15 22. The method of claim 21, wherein said first nucleic acid is labeled with a radiolabeled amino acid.

23. The method of claim 21, wherein said affinity tag is an affinity tag comprising a biotin.

24. The method of claim 23, wherein said antibody is a monoclonal antibody.

20 25. The method of claim 23, wherein said receptor is selected from the group consisting of a transferin receptor and an insulin receptor.

26. The method of claim 25, wherein said receptor is a transferrin receptor.

25 27. The method of claim 26, wherein the carboxyl terminal of said first nucleic acid is amidated.

28. The method of claim 1, wherein said contacting comprising systemically administering said imaging reagent to a living organism.

29. The method of claim 28, wherein said organism is a mammal.

30. The method of claim 28, wherein said organism is a non-human mammal.

31. The method of claim 28, wherein said organism is a human.

32. An imaging reagent for *in vivo* labeling of a gene or gene product, said imaging reagent comprising a detectable label attached to a first nucleic acid that specifically hybridizes to a second nucleic acid transcribed from said gene, where said first nucleic acid is linked to a targeting ligand that binds a receptor on a cell comprising the blood brain barrier of a vertebrate and crossing said blood brain barrier.

33. The reagent of claim 32, wherein said targeting ligand is selected from the group consisting of an antibody that specifically binds to a receptor on a cell comprising the blood brain barrier, and a substrate specifically bound by a receptor on cell comprising the blood brain barrier.

34. The reagent of claim 33, wherein said targeting ligand is selected from the group consisting of insulin, transferrin, insulin-like growth factor I (IGF-I), insulin-like growth factor II (IGF-II), basic albumin, leptin, and prolactin.

35. The reagent of claim 33, wherein said targeting ligand is an antibody that specifically binds to a receptor selected from the group consisting of an insulin receptor, a transferrin receptor, an insulin-like growth factor I (IGF-IR) receptor, and insulin-like growth factor II receptor (IGF-IIR), and a leptin receptor.

36. The reagent of claim 32, wherein said first nucleic acid is linked to said targeting ligand by a linker or by an affinity tag.

37. The reagent of claim 32, wherein said first nucleic acid is linked to said targeting ligand by an affinity tag comprising a biotin and a molecule that binds to biotin.

38. The reagent of claim 37, wherein said molecule that binds to biotin is selected from the group consisting of an avidin, a streptavidin, and an anti-biotin antibody.

5 39. The reagent of claim 37, wherein said first nucleic acid is a peptide nucleic acid.

40. The reagent of claim 39, wherein the carboxyl terminal of said first nucleic acid is amidated.

41. The reagent of claim 37, wherein said first nucleic acid is an antisense peptide nucleic acid.

10 42. The reagent of claim 37, wherein said first nucleic acid bears a protecting group.

43. The reagent of claim 37, wherein said first nucleic acid is a peptide nucleic acid having an amidated carboxyl terminal.

15 44. The reagent of claim 32, wherein said detectable label is selected from the group consisting of an radioactive label, a magnetic label, a spin label, an enzymatic label, a colorimetric label, and a fluorescent label.

45. The reagent of claim 32, wherein said nucleic acid is labeled with a radiolabeled amino acid.

20 46. The reagent of claim 45, wherein said radiolabeled amino acid is a tyrosine labeled with  $^{125}\text{I}$ .

47. The reagent of claim 45, wherein said radiolabeled amino acid is a lysine labeled with  $^{111}\text{In}$ .

25 48. The reagent of claim 32, wherein said gene is a gene that encodes a molecule selected from the group consisting of a receptor, and enzyme, a structural protein, and a transcription factor.

49. The reagent of claim 32, wherein:

said first nucleic acid is a peptide nucleic acid;  
 said targeting ligand is an antibody that specifically binds to a  
 receptor on a cell comprising the blood-brain barrier; and  
 said first nucleic acid is attached to said targeting ligand through an  
 5 affinity tag.

50. The reagent of claim 49, wherein said antibody is a monoclonal  
 antibody.

51. The reagent of claim 50, wherein said imaging reagent comprises a  
 radioactive label or a magnetic label.

10 52. The reagent of claim 51, wherein said first nucleic acid is labeled  
 with a radiolabeled amino acid.

53. The reagent of claim 51, wherein said affinity tag is an affinity tag  
 comprising a biotin.

15 54. The reagent of claim 53, wherein said antibody is a monoclonal  
 antibody.

55. The reagent of claim 53, wherein said receptor is selected from the  
 group consisting of a transferrin receptor and an insulin receptor.

56. The reagent of claim 55, wherein said receptor is a transferrin  
 receptor.

20 57. The reagent of claim 56, wherein the carboxyl terminal of said first  
 nucleic acid is amidated.

58. A kit for *in vivo* imaging of a gene or a gene product in a brain cell,  
 said kit comprising a container containing an imaging reagent comprising a detectable  
 label attached to a first nucleic acid that specifically hybridizes to a second nucleic acid  
 25 transcribed from said gene, where said first nucleic acid is linked to a targeting ligand that  
 binds a receptor on a cell comprising the blood brain barrier of a vertebrate and crossing  
 said blood brain barrier.

59. A kit for imaging a gene or a gene product in a brain cell, said kit comprising a container a nucleic acid that specifically hybridizes to said gene or to a nucleic acid transcribed from said gene attached to an affinity tag; and a container containing a targeting ligand that is capable of binding a receptor on a cell comprising the blood brain barrier of a vertebrate and crossing said blood brain barrier, where said targeting ligand is attached to an affinity tag such that when said nucleic acid is contacted to said targeting ligand the nucleic acid attaches to the targeting ligand by binding of the affinity tags.

60. The kit of claim 59, wherein said nucleic acid is a peptide nucleic acid.

61. The kit of claim 59, wherein said nucleic acid is labeled with a detectable label.